FRebekah R. Conroy, Esq.
STONE CONROY LLC
25A Hanover Road, Suite 301
Florham Park, New Jersey 07932
Telephone: (973) 400-4181
rconroy@stoneconroy.com

Attorneys for Defendants

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

PAR PHARMACEUTICAL, INC., PAR STERILE PRODUCTS, LLC, and ENDO PAR INNOVATION COMPANY, LLC, Plaintiffs, v. AMNEAL EU, LTD., AMNEAL PHARMACEUTICALS COMPANY GmbH AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL BIOSCIENCES LLC, and AMNEAL PHARMACEUTICALS PVT. LTD, Defendants.	Case No. 3:20-cv-18322 [redacted]

AMNEAL EU, LTD., AMNEAL PHARMACEUTICALS COMPANY GmbH AMNEAL PHARMACEUTICALS OF NEW YORK, LLC, AMNEAL BIOSCIENCES LLC, AND AMNEAL PHARMACEUTICALS PVT. LTD'S REPLY IN SUPPORT OF THEIR MOTION TO DISMISS PLAINTIFFS' AMENDED COMPLAINT

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Other Authorities

I. Introduction

Par attempts to maintain its infringement allegations by ignoring the steps of its patented methods and conflating them with the old, FDA-approved methods of using vasopressin. However, there can be no dispute that the currently approved use of vasopressin to treat septic and post-cardiotomy shock is *not the same* as the patented methods. Par itself distinguished between the FDA-approved methods of using vasopressin to treat septic and post-cardiotomy shock and the patented methods in (i) pleadings before this Court; (ii) its patents and before the Patent Office to obtain those patents; and (iii) its label amendment to the FDA. Contrary to Par's assertions, the infringement inquiry cannot be simplified for purposes of jurisdiction. Section 271(e) states that it shall be an act of infringement to submit an ANDA for a product "the use of which is claimed in a patent." The patented methods here include steps beyond the old, FDA-approved use of vasopressin for the treatment of septic and post-cardiotomy shock. Par ignores these required steps and treats them as entirely irrelevant to Par's ability to maintain an infringement suit. This cannot be correct, and Par's section 271(e) claims should be dismissed.

Par's section 271(b) claims are also deficient and depend on speculative future events. Par's Opposition attempts to downplay the unknown fate of Par's requested amendment by arguing that Par's infringement allegations do not depend on Amneal amending its labels. Par instead focuses its infringement arguments on

Amneal merely selling its proposed ANDA products as generic substitutes of Par's VASOSTRICT product. The Federal Circuit has held, however, that marketing a product as bioequivalent to another "cannot reasonably be interpreted as an act of infringement (induced or otherwise) with respect to a patent on an unapproved use." *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1364-65 (Fed. Cir. 2003). Par's allegations to the contrary are speculative and are not sufficiently imminent or certain to support a declaratory judgment claim of infringement.

As a result, Par's complaint should be dismissed in its entirety.

II. Par Attempts to Preserve Its Infringement Allegations by Ignoring the Steps of Its Patented Methods and Improperly Conflating Those "New" Methods with the Old, FDA-Approved Methods of Using Vasopressin

As set forth in Amneal's motion, Par cannot maintain claims of infringement under 35 U.S.C. § 271(e) if the ANDA does not seek approval to market a product to be used according to the patented methods. *AstraZeneca Pharm., LP v. Apotex Corp.*, 669 F.3d 1379 (Fed. Cir. 2012); *Warner-Lambert*, 316 F.3d at 1358–59. Under section 271(e), Par's allegations can stand only if Amneal seeks approval of a drug "the use of which is claimed in a patent," and thus requires a comparison of Amneal's proposed labels to the patent claims. But Par does not, and cannot, allege that Amneal is seeking approval to market vasopressin for use with patients identified as having AA or AT genotypes in accordance with the dosing regimens claimed in the asserted patents. As Par acknowledges, Amneal instead seeks

approval to market its proposed product for the [redacted]. (Doc. No. 20 at 5.)

Yet, Par argues that "Amneal seeks approval to market its vasopressin products for the ***exact same uses*** claimed in the Patents in Suit: [redacted]" (Doc. No. 20 at 14 (emphasis added); *see also id.* at 1 ("Amneal seeks approval for the use of vasopressin to [redacted] which is the same use recited in the asserted patent claims.").) Par is wrong in completely ignoring the elements of the claims in the asserted patents regarding the specified patient populations and the claimed dosage ranges, and is purposely conflating the old and allegedly new methods in its attempt to maintain this action. In various contexts, including in its pleadings before this Court, its patents, and its amended label, Par has recognized the differences between its patented methods and [redacted] that appears in Amneal's proposed labels. Par should not be permitted to treat the patented methods as different from the FDA-approved methods for its own benefit (for example, in securing its patents), and then conflate these different methods in its attempt to maintain this patent infringement action.

Par's pleadings demonstrate that the patented methods are different from the old FDA-approved methods. Par's assertion that Amneal seeks approval to market its vasopressin products for the uses claimed in the '435 and

'278 patents is belied by contradictory statements in its pleadings. Par admits that Amneal is seeking approval to sell its ANDA products [redacted] and states that VASOSTRICT (approved in 2014) is "commonly used" to treat septic shock and post-cardiotomy shock in hospital emergency rooms and ICUs. (Doc. No. 14, ¶ 30; Doc. No. 20 at 2, 5.) In contrast, Par refers to the patented methods as "new, innovative treatment regimens." (Doc. No. 20 at 4; *see also* Doc. No. 14, ¶ 41 ("These innovative treatment regimens represent an important medical advances [sic] in the way patients suffering from septic shock and post-cardiotomy shock can and should be treated with vasopressin.").) Par sought and obtained a patent for "new" and "improved" methods of using vasopressin, distinct from the uses of vasopressin that doctors have used for years. Par claims to have "unexpectedly" noticed that patients with specific genotypes need higher doses of vasopressin than previously used, and explains the differences between the old methods of treating septic shock and post-cardiotomy shock and its "new" patented methods in its Amended Complaint. (Doc. No. 14, ¶¶ 37-41.)

Here, as reflected in Amneal's proposed product labels, Amneal is seeking FDA approval to market vasopressin in accordance with "commonly used" (and unpatented) methods [redacted]. Amneal is not seeking approval to market vasopressin for use with patients who have been

identified as having AA or AT genotypes in accordance with the "new" dosing regimens claimed in the '435 and '278 patents, and Par does not allege otherwise.

Par's patents distinguish between the patented methods and the prior-art, FDA-approved methods of using vasopressin. Although Par now claims that the asserted patents are directed to the treatment of septic and post-cardiotomy shock (*see* Doc. No. 20 at 1, 14), that is not what Par told the Patent Office. Par recognized in the Background section of the asserted patents that the use of vasopressin to treat septic and post-cardiotomy shock was in the prior art: "VASOSTRICT® (vasopressin injection, USP) was approved by the United States Food and Drug Administration in 2014 to increase blood pressure in adults with vasodilatory shock (e.g., post-cardiotomy or sepsis) who remain hypotensive despite treatment with fluids and catecholamines." (Doc. No. 14, Ex. A at 1:20-25; Ex. B at 1:26-31.) The patents also cited various prior art references teaching the use of vasopressin to treat septic and post-cardiotomy shock. (*See, e.g.*, Doc. No. 14, Ex. B at 1 (*citing* Argenziano et al.; "A prospective randomized trial of arginine vasopressin in the treatment of vasodilatory shock after left ventricular assist device placement" Circulation; 1997; 96 (9 Suppl); pp. 286-290).) These methods of using vasopressin for vasodilatory shock had been used by doctors for decades and are not "the use of which is claimed in a patent." 35 U.S.C. § 271(e).

In contrast, Par summarized its patented methods as follows: "The treatment methods described herein generally comprise determining whether the patient is the TT, AA, or AT genotype, and then administering a dosing regimen of vasopressin based on genotype." (Doc. No. 14, Ex. A at 2:29-32; Ex. B at 2:35-38.) Par does not and cannot allege that Amneal is seeking approval to market a product which includes "administering a dosing regimen of vasopressin based on genotype." Amneal only seeks approval to market vasopressin products to be used [redacted]. Par cannot have it both ways: it cannot tell the Patent Office that patented methods are different from the prior-art FDA-approved methods, and then gloss over those differences here to maintain its patent infringement action against Amneal.

In seeking FDA approval to amend the VASOSTRICT label, Par recognized that the patented methods differ from the FDA-approved methods of using vasopressin. Despite its current arguments blurring the lines between the old, FDA-approved indication for using vasopressin and its allegedly novel methods, Par recognized that its patented methods are not included in the FDA-approved label for VASOSTRICT. The currently FDA-approved label contains instructions for using vasopressin to treat septic and post-cardiotomy shock. (Doc. No. 14, ¶ 24.) Par has sought to amend its label "to include new instructions concerning the dosage and administration of VASOSTRICT® in view of the

important, newly discovered information concerning the improved methods of administering VASOSTRICT® to patients with AA or AT genotypes." (Doc. No. 14, ¶ 42; Doc. No. 20 at 4.) If the patented methods are the same as the currently FDA-approved methods, as Par alleges, Par would not have needed to amend its label or seek additional FDA approval for the patented methods.

Moreover, as Par notes, FDA regulations require an NDA sponsor to "submit to FDA information on all patents claiming . . . a method of using that drug." (Doc. No. 14, ¶ 14; *see* 21 U.S.C. 355(b)(1)(A)(viii) (NDA sponsor must submit information on patents "for which a claim of patent infringement could reasonably be asserted").) The FDA regulations further require that, in identifying the types of method patents that need to be identified, "the applicant must submit information only on those patents that claim ***indications or other conditions of use*** for which approval is sought or has been granted in the NDA." 21 C.F.R. § 314.53(b)(1) (emphasis added).[1] The patents asserted here are not listed in the

[1] Notably, this requirement is not limited to only the conditions treated by the drug, but extends to the other conditions of use of the drug, such as dosing regimens or patient population. This process of providing patent information to the FDA for listing in the Orange Book is an integral part of the litigation scheme established by the Hatch-Waxman Act. Once a patent is listed in the Orange Book, any later ANDA applicant must file a certification regarding the patent, which triggers the deadline for the NDA holder to pursue patent litigation with the benefit of a 30-month stay of FDA approval of the ANDA. *See* 21 U.S.C. § 355(j). Par argues that "use" supporting jurisdiction is somehow limited to only the *indications* in the label. (Doc. No. 20, 13-14.) But it would be incongruous if the FDA required submission of information regarding patents covering "indications and other

Orange Book because the patented methods are not FDA approved and do not claim indications or other conditions of the use of vasopressin that are set forth in Par's FDA-approved label. Par recognizes as much: the asserted patents ***will be*** listed in the Orange Book "***upon approval of the label change***" adding reference to the claimed patient population and dose ranges. (Doc. No. 14, ¶ 43 (emphasis added).) Thus, while Par claims this is an infringement action under the Hatch-Waxman Act, it is not. Neither the '435 patent nor the '278 patent are listed in the Orange Book and cannot support Par's §271(e)(2) claims. *See Eisai Co. v. Mutual Pharm. Co.*, No. 06-cv-03613, 2007 WL 4556958 at *14 (D.N.J. Dec. 20, 2007) (granting defendants' motion to dismiss because plaintiffs, "as a matter of law, cannot maintain an infringement action pursuant to 35 U.S.C. § 271(e)(2) where the allegedly infringed patent was not listed in the Orange Book for the drug at issue and the ANDA contained no Paragraph IV certification against the patent.").

There can be no dispute that the currently FDA-approved use of vasopressin to treat septic and post-cardiotomy shock is *not the same* as the patented methods specifying specific patient populations and dosing regimens. Although Par asserts in its opposition brief that the FDA-approved methods are the same as the patented

---

conditions of use" for the purposes of triggering Hatch-Waxman litigation, but courts ultimately only looked at the "indications" to determine whether a ANDA seeks approval for a drug "the use of which is patented." 35 U.S.C. § 271(e).

methods, Par's amended complaint nowhere contains that erroneous assertion. In other words, Par has not and cannot allege that Amneal is seeking FDA approval to market a vasopressin product to be used in accordance with the patented methods, i.e. administering certain dosing regimens to patients with AA or AT genotypes. Because Par's infringement allegations are untethered to patented methods, Par has failed to plead a plausible claim to relief under section 271(e)(2) claims, and the Court should dismiss Par's claims under FED. R. CIV. P. 12(b)(6).

There is also no justiciable controversy between the parties related to the asserted patents because Par cannot point to any evidence that Amneal has engaged in any "meaningful preparation" for making a product that will infringe the asserted patents. *Cat Tech LLC v. TubeMaster, Inc.*, 528 F.3d 871, 881 (Fed. Cir. 2008). Par has not alleged—and cannot allege—that Amneal has sought to amend its label to include reference to the patented methods or is currently preparing to market its product with reference to such unapproved methods. The only allegations that Par can make regarding Amneal's preparation is that Amneal may—at some unknown point in the future—amend its label (Doc. No. 14, ¶ 51) and that Amneal may market its products once they are approved (Doc. No. 14, ¶ 52). These allegations are insufficient to support a claim for a declaratory judgment. *Eisai*, 2007 WL 4556958 at *18 (finding the controversy insufficiently immediate for declaratory judgment). Thus, Par's complaint must be dismissed.

III. Par's Inducement Claims Are Speculative and Insufficient to Sustain This Action

In its amended complaint, Par discussed FDA labels, explained how it has sought FDA approval to amend the VASOSTRICT label, and speculated that Amneal would have to amend its labels—all in support of its infringement allegations. Amneal pointed out the flaws in Par's infringement claim in its motion to dismiss. (Doc. No. 18 at 6-13.) In its Opposition, Par does not dispute that the FDA has not approved the amendment to the VASOSTRICT label to include reference to the claimed patient population and dose range. Not only is Par unable predict *when* the FDA will act on Par's request, Par cannot predict *whether* the FDA will allow such an amendment. Par's claim that Amneal will need to amend its label is similarly speculative. Par cannot say with any certainty what the FDA will require as a result of Par's request to amend the VASOSTRICT label.

As a result, Par pivots and argues that Amneal will induce infringement of the asserted patents by selling its proposed vasopressin product to be used in the same manner as VASOSTRICT.[2] Importantly, Par does not allege that Amneal is currently preparing to market or will affirmatively market its proposed product for use according to the claimed methods in the absence of FDA approval of these

[2] For purposes of this motion, Amneal does not attempt to disprove the false allegations in Par's complaint. Amneal reserves the right to dispute the accuracy of Par's allegations in due course.

methods. Both Par and Amneal are prohibited from marketing a drug for a use that is not approved by the FDA. *See, e.g.*, 21 U.S.C. § 351. Instead, Par alleges that it will market VASOSTRICT for use according to the patented methods and convince doctors to use those methods, and in turn, Amneal's proposed products will be used in the same manner. Par states that its inducement allegations are not dependent on *Amneal* amending its label, but fails to explain how Par will legally market VASOSTRICT for use according to the patented methods when it is unclear whether the FDA will approve such methods of using VASOSTRICT.

Without FDA approval of the patented methods, Par cannot market VASOSTRICT for use according to the patented methods. *See, e.g.*, 21 U.S.C. § 351. If VASOSTRICT can only be marketed for the currently FDA-approved methods of using vasopressin to treat septic and post-cardiotomy shock—without reference to using certain dosing regimens for certain genotypes—then Amneal's sale of its proposed generic products as a substitute for VASOSTRICT could not induce anyone to use the patented methods. Without FDA approval of the patented methods, Amneal's marketing and selling its proposed product as a generic equivalent of VASOSTRICT "is a perfectly lawful step" and cannot form the basis for Par's inducement claims. *See Organon, Inc. v. Teva Pharmaceuticals, Inc.*, 244 F. Supp. 2d 370, 379 (2002) (Defendants' marketing of "their product as an

across-the-board substitute for [the branded product] for all uses" "is a perfectly lawful step, created and regulated by the FDA").

Further, Par's inducement allegations rely completely on the actions of third parties that Amneal does not control. The Federal Circuit has repeatedly held that mere knowledge that someone may perform the claimed method is not enough to be liable for induced infringement. *Warner-Lambert,* 316 F.3d at 1364-65; *Takeda Pharmaceuticals U.S.A. v. West-Ward Pharmaceutical Corp.*, 785 F.3d 625, 631-32 (Fed. Cir. 2015) ("label must encourage, recommend, or promote infringement" to induce infringement). To induce infringement, Amneal must have specific intent and take action to induce someone to perform the claimed methods. *Warner-Lambert,* 316 F.3d at 1365 ("mere knowledge of possible infringement by others does not amount to inducement; specific intent and action to induce infringement must be proven."). Here, the only Amneal action Par alleges is Amneal marketing its products as substitutes for VASOSTRICT. Assuming this allegation to be true for purposes of this motion only, such marketing would *not* constitute an affirmative act to encourage infringement because absent FDA approval, Par cannot market VASOSTRICT for use in the patented methods.

In addition, Par has failed to plead sufficiently concrete facts of direct infringement, i.e., that doctors will actually perform the claimed methods. Par has not alleged that the current uses of vasopressin are dangerous or lacking in some

way. In fact, as Par admits, it has sold VASOSTRICT for use according to the FDA approved methods since 2014. (Doc. No. 14, ¶ 21.) Despite alleging that failure to use the patented methods could result in "sub-optimal treatment" (Doc. No. 14, ¶ 53), Par does not allege that doctors are currently practicing the patented methods in their use of VASOSTRICT or that doctors will change their practices in order to use the patented methods. And on their face, Par's allegations are simply not plausible. Par alleges that vasopressin is used in "vasodilatory shock, including septic shock and post-cardiotomy shock, is a life-threatening condition that need to be treated on an ***emergent*** basis." (Doc. No. 14, ¶ 53 (emphasis added).) But the patented methods require the patient's genotype, which takes hours if not days to determine. Par nowhere explains how a doctor can practice the patented method, including determining the patient's genotype, and treat vasodilatory shock on an emergent basis.[3] Therefore, Par's infringement allegations, based on speculative facts and implausible circumstances for direct infringement, are insufficient to maintain this action.

IV. The Court Can and Should Consider Amneal's Proposed Labels

Par's arguments that the Court should disregard the Exhibits to Amneal's Motion to Dismiss—the proposed labels to be included with Amneal's ANDA

[3] The Court is "not compelled to accept [Par's] 'unsupported conclusions and unwarranted inferences,' or '[its] legal conclusion couched as a factual allegation.'" *Baraka v. McGreevey*, 481 F.3d 187, 195 (3d Cir. 2007).

products—are misplaced. As Amneal explained in its Motion to Dismiss, courts may consider documents "integral to or explicitly relied upon in the complaint . . . without converting the motion to dismiss into one for summary judgment." *Borough of Moosic v. Darwin Nat'l Assurance Co.*, 556 F. App'x 92, 95 (3d Cir. 2014) (quoting *In re Burlington Coat Factory Sec. Litig.*, 114 F.3d 1410, 1426 (3d Cir. 1997) (internal quotations omitted)). This is precisely the situation here.

Setting aside Par's characterization of its infringement allegations set forth in its Opposition, the allegations in the complaint depend on Amneal's proposed labels and speculation that the FDA will require Amneal to include reference to the claimed methods. (*See, e.g.*, Doc. No. 14, ¶¶ 48, 51, 54.) Unlike the cases that Par cites, Par's reliance on Amneal's proposed labels is not general in nature. The plausibility of Par's infringement allegations turn on the content of what will be included in Amneal's proposed labels, making them exactly the type of "integral" documents that courts are permitted to consider.

Moreover, Par does not claim that consideration of Amneal's proposed labels would be prejudicial to Par. Courts have noted that the primary concern with considering documents outside the complaint is lack of notice to the plaintiff, but that is not an issue here. *See Burlington*, 114 F.3d at 1426 ("[T]he primary problem raised by looking to documents outside the complaint—lack of notice to the plaintiff—is dissipated where plaintiff has actual notice . . . and has relied upon

these documents in framing the complaint." (internal quotations omitted).) As Par stated in its Amended Complaint, the FDA requires that an ANDA applicant copies the approved label. (Doc. No. 14, ¶ 16.) It does not matter that Par did not specifically cite to Amneal's labels; Par had notice of and relied on the contents of Amneal's labels in framing its complaint. *Burlington,* 114 F.3d at 1426.

The cases on which Par relies are inapplicable here. In *Cima Labs, Inc. v. Actavis Grp. HF*, the complaint did not rely on the content of the label or any other part of the ANDA. No. 07-cv-893 (DRD), 2007 WL 1672229, at *4 (D.N.J. June 7, 2007). Similarly, in *Par Pharma., Inc. v. Hospira, Inc.*, as Par recognized, references to the ANDA in the Complaint were "limited to the fact of the ANDA's filing and to summarize its contents as described in the Paragraph IV notice letter." No. 17-cv-944-JFB-SRF, 2018 WL 3343238, at *2 (D. Del. May 11, 2018). Here, on the other hand, Par made allegations regarding the specific contents of the labels (how Amneal will instruct doctors to use its proposed products), making them appropriate for consideration in this motion.

V. Conclusion

For the reasons set forth in Amneal's Motion to Dismiss and discussed above, Par's Complaint against Amneal should be dismissed.

Respectfully submitted,

/s/ Rebekah R. Conroy
Rebekah R. Conroy
STONE CONROY LLC
rconroy@stoneconroy.com
25A Hanover Road, Suite 301
Florham Park, NJ 07932
(973) 400-4181

Of Counsel:
Huiya Wu
Linnea Cipriano
GOODWIN PROCTER LLP
The New York Times Building
620 Eighth Avenue
New York, NY 10018
hwu@goodwinlaw.com
lcipriano@goodwinlaw.com
Tel: (212) 813-8800